DESIGN, FABRICATION AND TESTING OF AN ENDOVASCULAR MECHANICAL THROMBECTOMY DEVICE

An Undergraduate Research Scholars Thesis

by

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ABSTRACT

Design, Fabrication, and Testing of an Endovascular Mechanical Thrombectomy Device.
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Stroke is a leading cause of death and debilitation in the United States, with ischemic stroke in particular affecting hundreds of thousands of people every year. Treatment options for ischemic stroke have several limitations. Among ischemic stroke treatment options, mechanical thrombectomy offers significant advantages, including a longer time window for treatment. However, these devices also have limiting factors such as limited maneuverability and poor performance in certain vessel geometries. The focus of this work is to discuss the design and testing of an alternative mechanical thrombectomy device to be used for ischemic stroke treatment. This device will aim to remove some of the limiting factors that currently affect mechanical thrombectomy devices.

Fabrication of the device was accomplished through a combination of shape memory polymer foam and nitinol tubing attached to a guidewire. Characterization of the device was achieved by utilizing a set of tensile testing procedures and a set of *in vitro* mechanical thrombectomy procedures. Retraction force was recorded during some of the *in vitro* procedures for comparison to the tensile data. Average tensile force required to cause device failure was more than 2.75 times the peak retraction force seen in any trial. *In vitro* thrombectomy was performed

successfully in all attempted trials for a specific geometry, suggesting that this device has potential as an alternative treatment option. Further in vitro thrombectomy trials to compare the design to current FDA-approved mechanical thrombectomy devices and a set of preclinical tests to show effectiveness in an animal model would validate the design and pave the way for clinical studies.

ACKNOWLEDGMENTS

I would like to thank some key people for their help, support and guidance in completing this undergraduate thesis.

Thank you to Dr. Duncan Maitland, who has provided me this exceptional opportunity and has helped guide me through the past two years of research in his lab. His support has inspired me to make research my career. Working in his lab has taught me more than sitting in any number of classes. I'll carry those lessons through the rest of my life.

Thanks also go to Dr. Andrea Muschenborn, who mentored me through my first year of undergraduate research. She showed me how the nuts and bolts of research work and gave me the chance to build cool things, something that every engineer dreams of. And, most importantly, she taught me that swearing at your experiments improves their outcome by a statistically significant percent.

Thanks to the other members of the Biomedical Device Lab for their support across the past couple of years. It helps tremendously to have a community of people behind you willing to help out when things get tough.

And finally, thanks to my family and friends who made coming home at the end of the day worthwhile.

NOMENCLATURE

SMP	Shape Memory Polymer
SMA	Shape Memory Alloy
FDA	Food and Drug Administration
rtPA	Recombinant Tissue Plasminogen Activator
KOH	Potassium Hydroxide
OD	Outer Diameter
ID	Inner Diameter
UV	Ultraviolet
PVC	Polyvinylchloride
T_g	Glass Transition Temperature

CHAPTER I

INTRODUCTION

Clinical motivation

Each year, a significant portion of Americans suffer a stroke, with 610,000 people affected by a new presentation of the disease and 185,000 faced with a recurring case. In fact, it is estimated that on average in the United States, every forty seconds a person has a stroke and every four minutes someone dies from a stroke [1]. Of these strokes, 87% are considered ischemic, where an embolus, usually a thrombus, blocks vital blood flow in an artery of the brain, potentially leading to brain damage, physical disability, or death. Figure 1 depicts a fluoroscopy of a blood clot lodged in a porcine vessel as would be seen in an ischemic stroke.

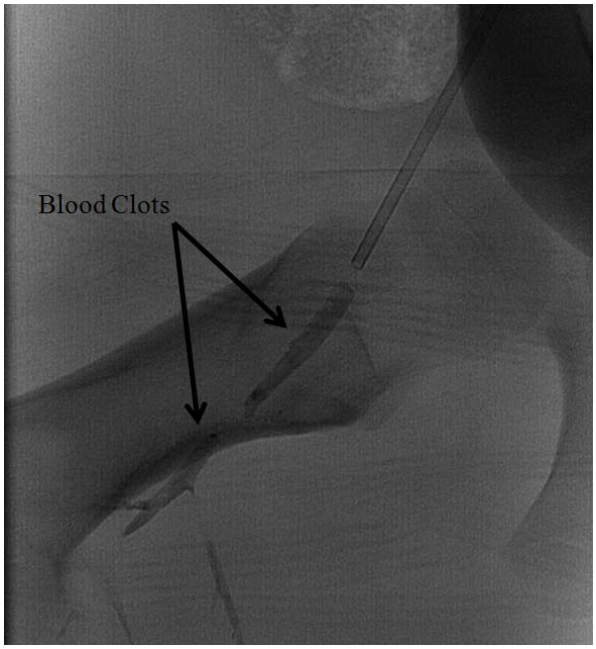

Figure 1. Fluoroscopy of thrombus injected into porcine artery. Clots formed in the carotid artery commonly break off and lodge in narrowed regions of the cerebral vasculature causing an ischemic stroke.

Standard treatment protocol involves administration of IV thrombolytics, typically recombinant tissue Plasminogen Activators (rtPA), which act to enzymatically dissolve blood clots present throughout the vascular system. Though rtPA is the standard treatment option, its use is limited to within 3 hours of symptom onset, requiring for an extremely quick recognition of the symptoms by the patient and for fast transportation to a hospital with proper diagnostic equipment and a neurology department. After 3 hours, administration of rtPA can lead to damage of endothelial cells in the ischemic region, which causes further damage to an area that is already afflicted. Also, treatment with rtPA can lead to a higher early mortality rate within the first week of symptom onset than that seen in untreated patients, though the long term mortality rate for the treated groups is significantly reduced [2]. The high early mortality rate is associated with the nearly tenfold increase in the risk of intracerebral hemorrhage for patients being treated with rtPA [3]. Use of intra-arterial thrombolytics has been examined, and though it shows promise, similar issues with a high initial rate of intracerebral hemorrhage have been documented [4].

In light of the difficulties seen in thrombolytic treatment, a recent wave of mechanical thrombectomy devices has become available as an alternative means of treatment. These devices are designed to be inserted endovascularly via a catheter to the sight of the blockage where they retrieve the obstruction [5-7]. Though these devices are novel and can be used in up to an 8 hour treatment time window, up until the past few years these devices have only been successful in restoring flow in a moderate percentage of cases and many of the clots were fractured during retrieval. In some devices, the goal is to disrupt the blood clot into smaller pieces that may then be aspirated through a vacuum catheter . For devices that do break up the clot, they run the risk

of distal embolization if the fragments created by the device that escape suction are large enough to cause further blockages. Small clot fragments can also serve as nucleation sites for the formation of larger blood clots.

Recently, more successful mechanical thrombectomy devices have included a high performing set of devices known as ‘stentreivers’, which act to instantly restore blood flow by expanding a stent within the blood clot. The stent is then used as a kind of net to retrieve the blood clot to a large catheter for aspiration and removal [8, 9]. Devices included under the ‘stentriever’ moniker have proven successful in many studies, albeit with some limiting factors. ‘Stentrievers’ typically have lengths of up to 40 mm which reduces their maneuverability in the tortuous cerebral vasculature, and the added length makes the distance by which the device needs to be advanced past the blood clot greater, compounding the issue. Additionally, these devices offer no material perpendicular to the vessel walls to catch any fragments that come off the main blood clot, and also, the lack of perpendicular material makes retrieving blood clots longer than the stents highly unlikely [10]. Blood clots are adhered to the vessel walls; therefore, if the stent is not long enough to expand through the entire length of the clot and break that adhesion, there is a possibility of device failure.

Research objectives

Because of these limitations, this study aims to design and test a novel mechanical thrombectomy device. The device consists of a combination of shape memory materials, which are materials that are created in an original shape, set in a secondary shape by heating or constraint, and then actuated by a stimulus to return to their original shape. Included in the

device will be both the shape memory alloy (SMA) nitinol and shape memory polymer (SMP) foam.

The incorporation of nitinol in the device is necessary to provide a sturdy backbone for holding the shape memory polymer foam in place. Nitinol is also a psuedoelastic material, which means that it can elastically recover from strains of up to 8 percent [11]. Because of this effect, a large radius nitinol piece is able to be included that will recover from the deformation of being placed into the lumen of the catheter. After recovery, it can provide axial force to pull the SMP foam into contact with the blood clot. The force of the nitinol pushing on the foam will lead to radial expansion of the foam, filling the vessel and preventing the clot from slipping around the device. Because of the ability to set the shape of nitinol through mechanical constraint and heat treatment, the nitinol piece can be produced in a geometry that collapses to a small radius after being forced into the lumen of a catheter. Pushing the nitinol piece out will allow it to recover its larger radius geometry.

SMP foams are important to the success of the device due to their shape memory properties and high compliance. SMPs are unique in their ability to exhibit the entropically driven shape memory effect. Heating these polymers above their glass transition temperature (T_g) gives the chains in the polymer enough energy to be mobile. Changing the geometry of the shape by crimping causes the linear orientation of chains through chain motion. Cooling the polymer while constrained removes the ability of the polymer chains to move, locking in the secondary geometry under un-strained conditions. Reheating the polymer, causes the chains to become mobile again, and due to the higher order caused by the crimping process, it becomes favorable

to return to the original shape to increase entropy. Additionally, the SMP foams used for the device can be crimped to 20% of their initial diameter and retain the ability to recover their initial geometry, providing an easy way to advance the foams through a catheter [12]. The polyurethane foams used for the study were plasticized by water and had a low T_g, which allowed their expansion from the crimped state by exposing them to blood. This allowed for the passive actuation of the foams, where, in the past, shape memory polymers have required a heat source to recover their initial geometry [13].

The high compliance of the SMP foams allows for the axial compression of the foam by the nitinol portion of the device to expand the foam radially, which ensures a large surface area of contact between the device and the blood clot. A larger surface area of the device in contact with the thrombus could serve to increase thrombus hold. The low radial expansion force of the SMP foams ensures that the endothelial layer of the vessel wall has as little chance of rupture or perforation as possible [14]. Figure 2 shows the concept for the device design.

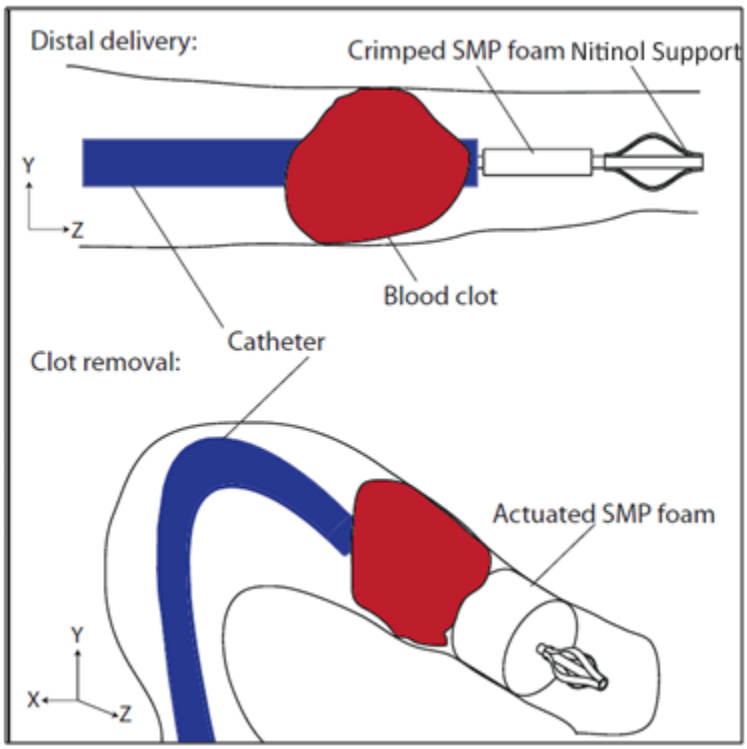

Figure 2. Device concept. Device is inserted past blood clot where shape memory and psuedoelastic effect of the materials used allow for expansion of device from catheter for large surface of contact [15].

There were several goals in designing the device. To improve on the length issue seen with the stent-like devices, one of the objectives of the project was to ensure the length of the device was less than 15 mm to allow for increased device maneuverability. To allow retraction of blood clots longer than the device and to help prevent distal embolization, the device was designed to provide a retrieval mechanism perpendicular to the blood vessel. As a qualitative measure of device success, it was also important to make sure the device could perform *in vitro* through a testing setup similar to what would be seen *in vivo*. Finally, it was important to ensure the failure force of the device would be higher than the retraction force required to retrieve a blood clot, in order to prevent the potential complications related to device fracture.

CHAPTER II

METHODS

Device fabrication

The first step in machining the device involved laser cutting a piece of nitinol tubing into a basic shape using an Excimer laser cutter (RapidX, Resonetics). In all cases, this basic shape consisted of a 7 mm section of 0.016” OD and 0.013” ID tubing cut with 4, 5 mm long axial slits with a 1 mm gap on each of the edges. The slits were spaced equally around the radius of the tubing.

After being cut with the Excimer laser, the nitinol tubes with slits were then placed over a 0.010” diameter nitinol wire and rolled on 600 grit sandpaper for 30 seconds to remove burs created by laser cutting. The nitinol pieces were then etched using 5 M Potassium Hydroxide (KOH) for 30 minutes at 120^{o} C while being stirred with a magnetic stirring bar [16]. They were also placed in a sonicator (3510, Branson) with 100% Isopropyl alcohol solution for 1 minute to remove any soluble dirt particles from the surface. The effects of these treatments can be seen in Figure 3.

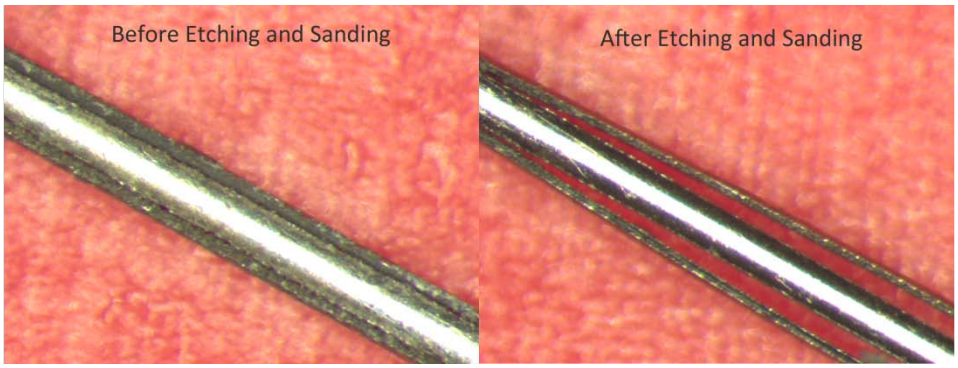

Figure 3. Effects of sanding and etching. Sanding and etching smoothed the surface of the device and removed large burs from the material that could potentially serve as stress concentrators.

This laser cut, sanded, and etched sample was then placed into an aluminum fixture which acted to compress the basic nitinol shape into the desired secondary flower-like geometry. The fixture was made of a sliding aluminum wedge placed within a hollowed-out channel in an aluminum block. A screw was placed into a threaded hole on one of the ends of the aluminum block to provide force to move the sliding component down the channel. Screws were also placed upright in the sliding piece and the aluminum block in threaded holes. A hole was then bored through the shank of each upright screw at the same height. To set the shape of the nitinol component cut using the Excimer laser, a wire was placed through the center of the tubing, which was subsequently placed through the holes on the two upright screws in the aluminum fixture. Washers were secured around the wire to hold it in place. By inserting the screw used to push the sliding aluminum piece, the tubing was compressed between the two sets of washers on each screw, which served to constrain the tubing into a compressed secondary geometry. Heating in a furnace at 550^{o} C, followed by quenching in room temperature water, set the unstrained shape to match the compressed secondary geometry. Figure 4 shows the process by which the device was shape set.

For later iterations of the device, the amount of axial compression was varied to affect the failure force and foam retention during tensile testing. Originally, the device was compressed from an axial length of 7 mm to 6.25 mm, but in later iterations was compressed from 7 mm to 5.75 mm of axial length.

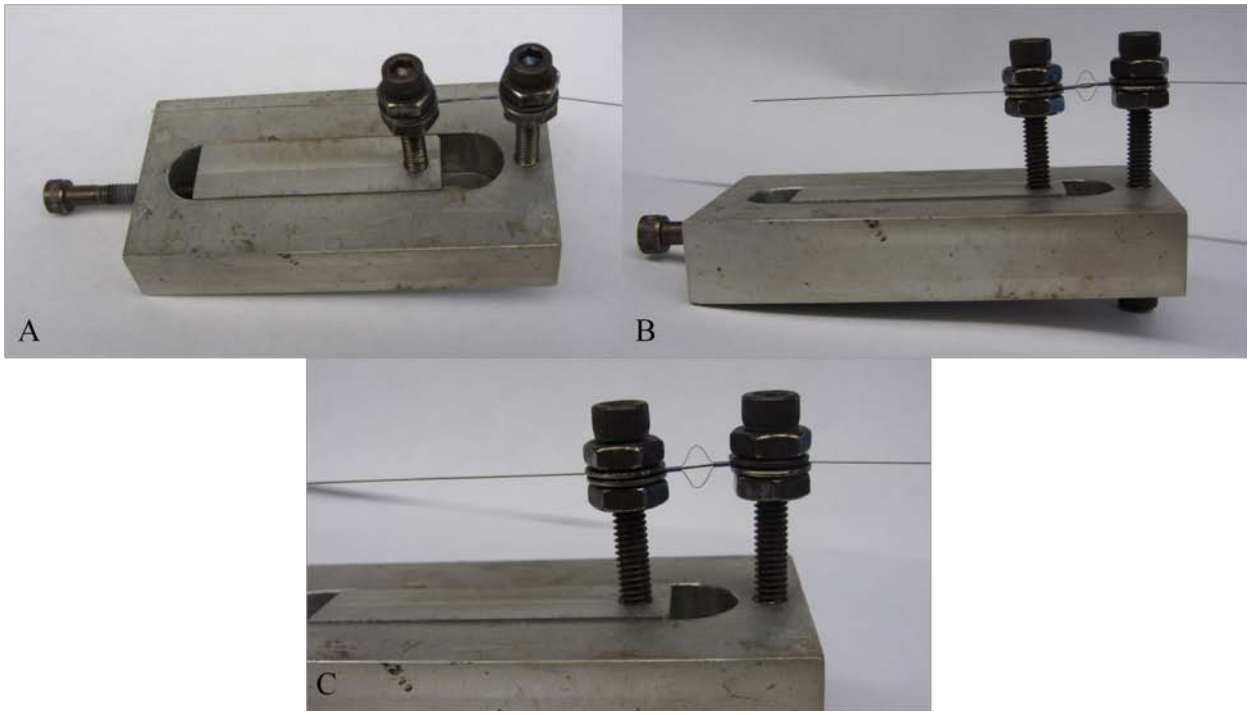

Figure 4. Shape setting the nitinol support piece. Pane A shows the tube placed between the faces of two washers. B shows the axially compressed tube as the screw on the right hand side is rotated inwards. C shows the final compressed support piece before it is placed in the furnace.

For later iterations of the device, sections of larger diameter nitinol tubing, referred to as collars, were used during the shape setting process to constrain and direct the compression of the nitinol to a configuration that served to reduce stress on the more fragile sections of the nitinol support piece. The collars placed around the nitinol tubing were typically 1.5 mm in length and 0.023" OD and 0.020" ID. Figure 5 depicts the collars in place on the support piece.

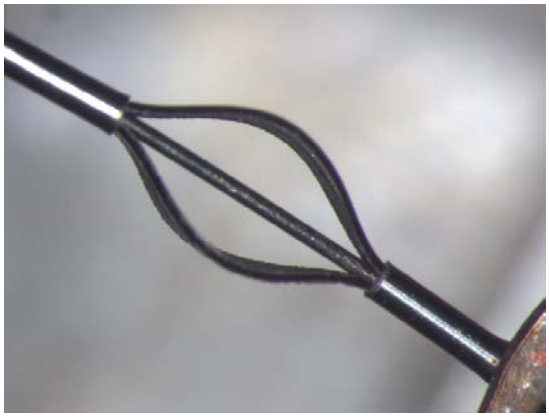

Figure 5. Constrained device with collars. The struts of the device were forced straight at the contact point between their ends and the uncut portion of the tubing. Stress was concentrated at the ends of the struts when collars weren't employed causing low force device failures.

This allowed the collar to cover part of the slit and direct the strain experienced during constraint away from the joint between the struts created by the laser and the solid part of the tubing. Without the collars, the device tended to crack at the joint of the tube and the struts. Figure 6 shows the cracks at the strut-tube interface without the collars present.

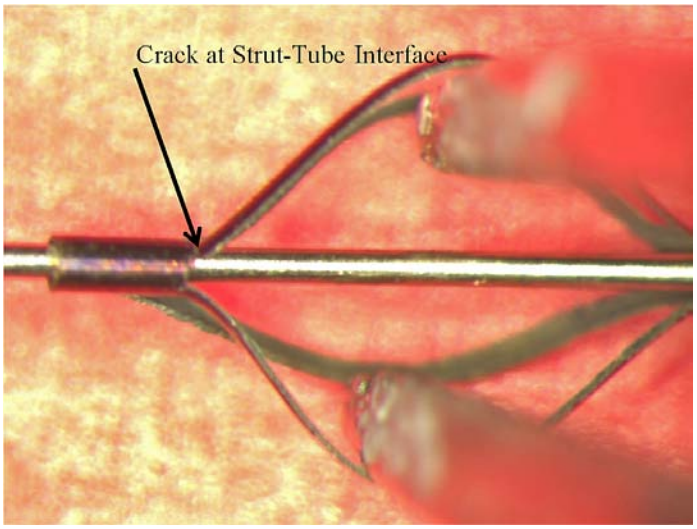

Figure 6. Cracks at strut-tube interface. As radial force was applied to the device, cracks became wider and more evident. Devices often failed after only three compression-expansion cycles.

The shape set component was then attached to a 5’ segment of 0.010” nitinol wire using a 1064 nm YAG laser welder (i990, LaserStar), which provided a stable backbone for transport of the device through the catheter. The device was only welded at the distal tip to allow for compression of the device when a force is applied to the proximal end, as seen in Figure 7.

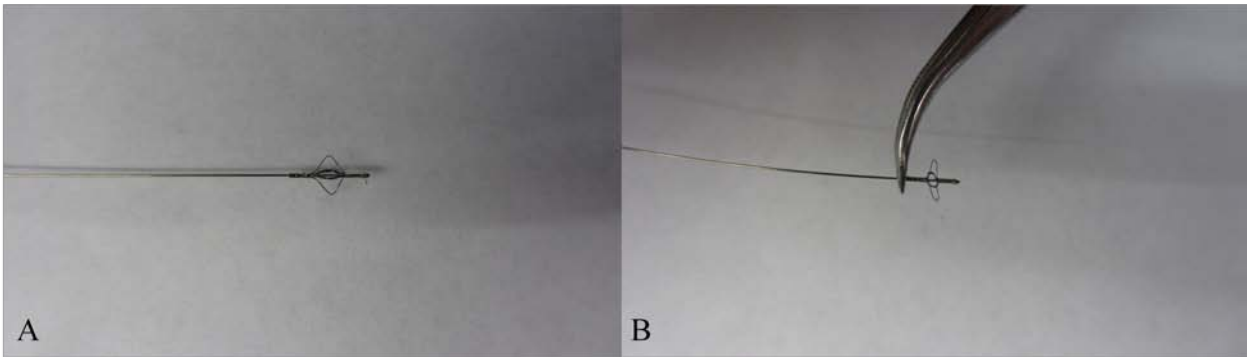

Figure 7. Axial compression on support piece. As the device is compressed from A to B, radial expansion occurs. Device is welded to the guidewire at the distal tip.

The nitinol wire used as the guidewire was heat treated before the welding in a furnace (Thermolyne, Thermo Scientific) set to 550^{o} C to reduce its stiffness at the distal tip. This was done to allow the device to better fit the contours of the vessel as it was retracted.

To further reduce stress at the joint between the strut and the rest of the nitinol tube, later iterations of the device had the collars used during the shape setting process welded onto the nitinol support piece of the device, as seen in Figure 8.

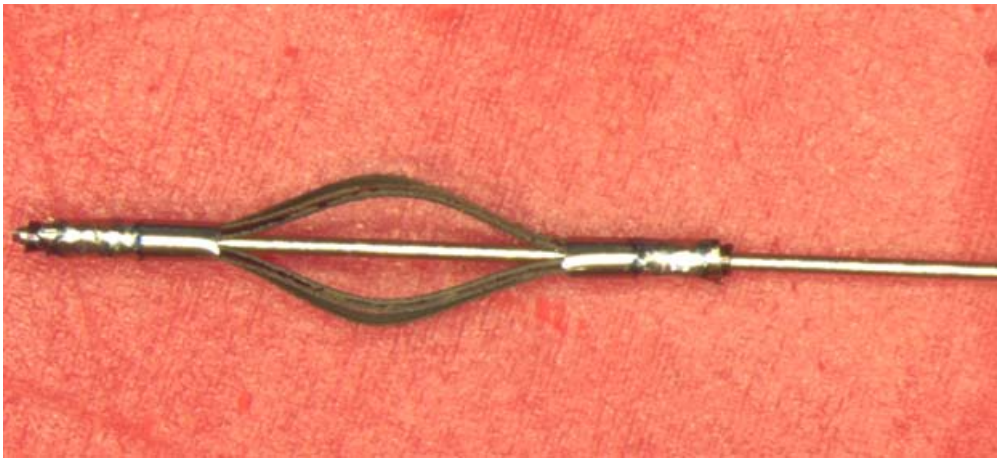

Figure 8. Support piece with welded collars. Collars helped keep the stress focused on the center of the struts. Without the collars, the struts were still able to deform to the point where stress was focused on the strut-tube interface.

After completing the attachment of the shape set nitinol components, a cylinder of SMP foam oversized to approximately 1.5 times the vessel diameter to be treated was placed over top of the nitinol wire and placed in position proximal to the nitinol flower. The targeted vessel was 4 mm in diameter, so a 6 mm diameter sample of foam was used in all cases. A 6 mm biopsy punch was used to remove the sample from a large block of foam. A razor blade was then used to cut the sample to an axial length of 5 mm. The SMP foam cylinder was then placed over a 0.010" Nitinol wire. This allowed the foam to be put into a stent crimper (SC250, Machine Solutions), where its diameter was drastically reduced to a new crimped geometry after being heated to 100^{o} C. The foam was then allowed to cool to room temperature over the course of 2 hours to set its secondary geometry. The foam was then able to be transferred from the crimping wire to the guidewire of the device. The crimped diameters of the foams used were approximately 1 mm in all cases. The SMP foams used were polyurethane based. Their synthesis is described by a previously reported method [12].

For one of the iterations of design utilized in tensile testing, the devices were constructed with the foam being epoxied to the shape set nitinol support piece. In those cases, UV curable, medical grade epoxy was spread around the proximal nitinol collar of the shape set nitinol piece using a cotton swab. The cylinder of foam was then placed around the epoxied portion and was secured to the shape set nitinol piece through attachment to the collar. The UV epoxy was then cured using a UV light (Series 1000, OmniCure).

The final step in fabrication of the device involved placing a pusher portion of nitinol tubing proximal to the SMP foam cylinder. Because the SMP foam is plasticized in water, it can expand as soon as it is placed in the flushed catheter. The pusher is included to provide pushing force on the face of the foam and keep it from sliding along the wire as the device is advanced. The pusher was constructed by welding a 2.5 mm piece of 0.016” OD and 0.013” ID nitinol tubing around the guidewire of the device. Then a larger diameter, similar length piece of tubing made from 0.023” OD and 0.020” ID nitinol was welded around the smaller piece of tubing to ensure the pusher could provide enough surface area to produce adequate force to move the expanding foam along the catheter. The distal end of the pusher was located ~13 mm from the tip of the guidewire to allow for the nitinol support piece to be compressed radially and expanded axially when placed in a catheter without interfering with the pusher or foam. The fully assembled device is shown in Figure 9.

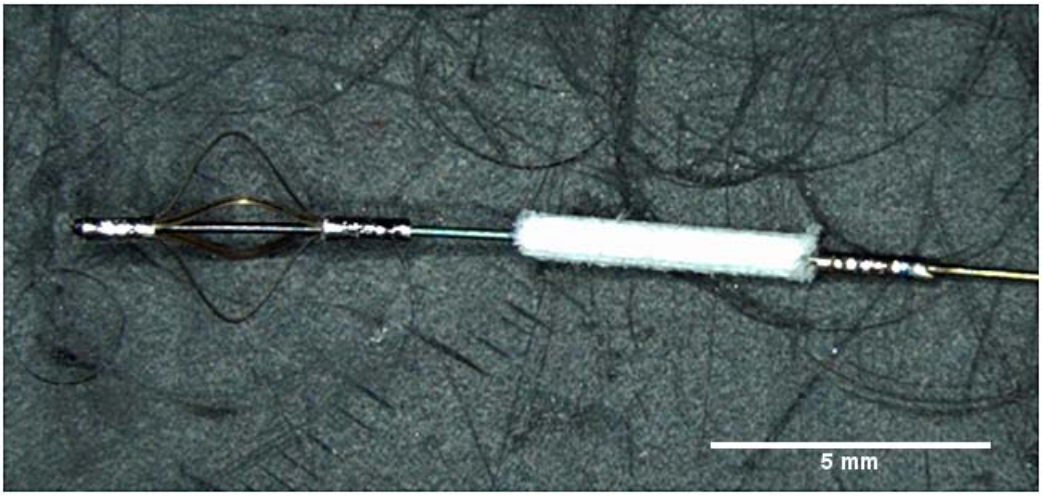

Figure 9. Assembled device. The nitinol support piece was compressed during pusher welding to make sure it did not interfere with the foam placement. After the proximal end of the pusher was welded, the foam was pushed to compress the support piece so the laser welder would not actuate the foam.

Failure testing

Failure testing of the device was undertaken using a tensile tester (MTS, Synergie, 50 N load cell). The device was fixed to the tensile tester by means of a clamp around the proximal tip of the wire while the rest of the wire portion of the device went through a conduit to ensure device alignment. The end of the alignment conduit acted as a stopper by providing a hole that was big enough to pass the guidewire and nitinol support piece but too small to pass the SMP Foam. Force caused by the tensile tester pulling on the wire compressed the foam portion and nitinol portion against the stopper until the device failed. Around the testing setup, a 37º C water bath was set up to provide the heat necessary to actuate the SMP foam to a larger diameter than that of the hole. The device was retracted at a rate of 75 mm/min until the device failed. Failure was evidenced by a sharp drop off in force being recorded by the tensile tester. Four different designs of the nitinol support piece were utilized in the tensile testing process to ensure optimization of the device. The best performing design was then reproduced for in vitro tests. Each set of failure

tests was carried out with a sample size of five. The pusher was not included on the devices used for failure testing to prevent the pusher from catching on the stopper. Figure 10 shows a schematic of the tensile testing setup.

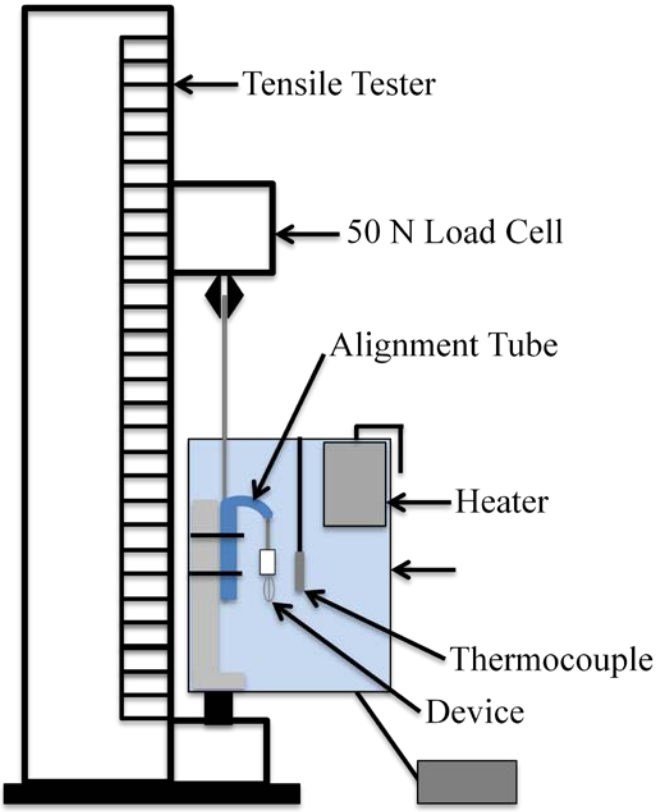

Figure 10. Failure testing setup. Device was pulled against alignment tube by tensile tester until failure occurred. Heater and thermocouple were used to keep water bath at 37^{o} C.

In vitro thrombectomy

In vitro tests were carried out in a flow loop created using a series of clear PVC tubing connected to a clear silicon bifurcation vessel model. A peristaltic pump brought 37^{o} C water from a water bath and emptied the water into a discharge container. Blood clots were prepared by mixing 10 mL of bovine blood with 25 IU of bovine thrombin, and one gram of barium sulfate [17]. During

each experiment, a blood clot that had been aged at room temperature over night was injected into the flow loop, where it lodged within a branch of the bifurcation model. Figure 11 shows a blood clot after it's been placed in the vessel model.

Figure 11. Blood clot lodged in silicone vessel model. Clot was pushed into place using syringe flow.

A 5 F catheter was deployed through a Luer lock, and its tip was placed distal to the blood clot. It was then flushed with body temperature water in an attempt to remove some bubbles from the setup. The device was then fed through the lumen of the catheter and advanced out of the catheter to allow for expansion of the foam. In some cases, a syringe filled with body temperature water was injected through the catheter around the device. This procedure was performed to flush out bubbles and aid in the expansion of the foam. Once the device was deployed, the catheter was retracted proximal to the blood clot, and the device was used to remove the blood clot. Only the best device from tensile testing was used for attempted *in vitro* thrombectomy trials. A successful trial was marked as retraction of the device past the

bifurcation in the vessel. After the device passed the bifurcation, flow was restored to the obstructed vessel, and the blood clot had a large amount of flow at an angle to the device contact surface, offering the greatest chance to dislodge the clot. Furthermore, in an *in vivo* study, once the device was retracted to a vessel of the diameter of the vessel past the bifurcation, a large diameter catheter would be used to aspirate the clot.

Retraction force

Retraction force tests were performed using the same flow loop from the *in vitro* thrombectomy test setup. The procedure for injecting the blood clots and putting the device in place for retraction through the Luer connection was repeated. The proximal tip of the wire was then affixed to the same clamp on the tensile tester through the same conduit used for alignment that was mentioned in the tensile testing procedure. Retraction force was then measured as the tensile tester pulled the device and blood clot through the *in vitro* thrombectomy setup at an extension of 75 mm/minute. Successful trials were marked with the same criteria as the previous *in vitro* studies. Figure 12 illustrates the general setup for the retraction force studies.

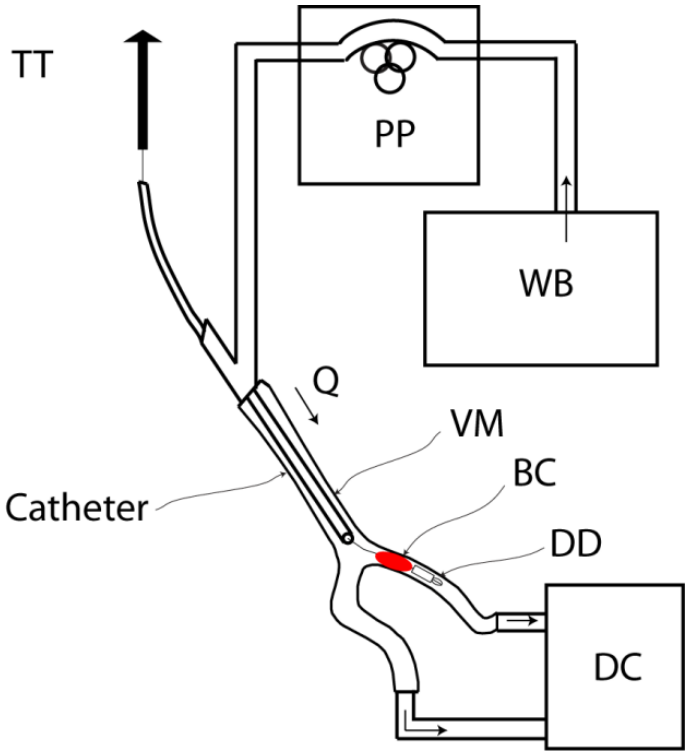

Figure 12. Retraction force measurement setup. TT – Tensile Tester, PP – Peristaltic Pump, WB – Water Bath, Q – Flow, VM – Vessel Model, BC – Blood Clot, DD – Distal Device, DC – Discharge Container. Tensile tester pulled device until manually told to stop when the trial either failed or succeeded.

CHAPTER III

RESULTS AND DISCUSSION

Tensile testing

After straining each of the four initial device designs to failure, the widely shape set device with no epoxy holding the foam emerged as the clear frontrunner, withstanding forces of on average 7.43±0.94 N. Figure 13 shows each tensile testing design and force versus retraction data. This option, device D from Figure 13, performed better than the other designs for a number of reasons. The first tested design, device A from Figure 13, lacked collars and was radially expanded to 2.5 mm. The lack of collars caused the device to fail at the joint between the strut and rest of the tubing in all cases. Because the collars directed the force to the middle of the struts, the second iteration of the device, device B from Figure 13, failed at an average force of 2.824±0.681 N versus an average failure force of 1.424±0.374 N for the device without collars. The device with a smaller shape set diameter allowed the foam to slip off during some of the cases, which caused immediate failure since there was no longer anything to keep the device from pulling through the stopper. The addition of widening the radius of the nitinol support piece to 4 mm prevented the foam from being able to come off of the support piece without the piece actually breaking in some way. Another solution to the foam coming off was attempted by using epoxy and is shown on device C in Figure 13. Epoxy was used to attach the foam to the nitinol support piece collars for one set of trials in an attempt to prevent this effect. However, the epoxy prevented the compression of the nitinol support piece and caused the device to fail prematurely. Figure 14 displays the maximum forces for each trial of each design and the average of all trials for each design.

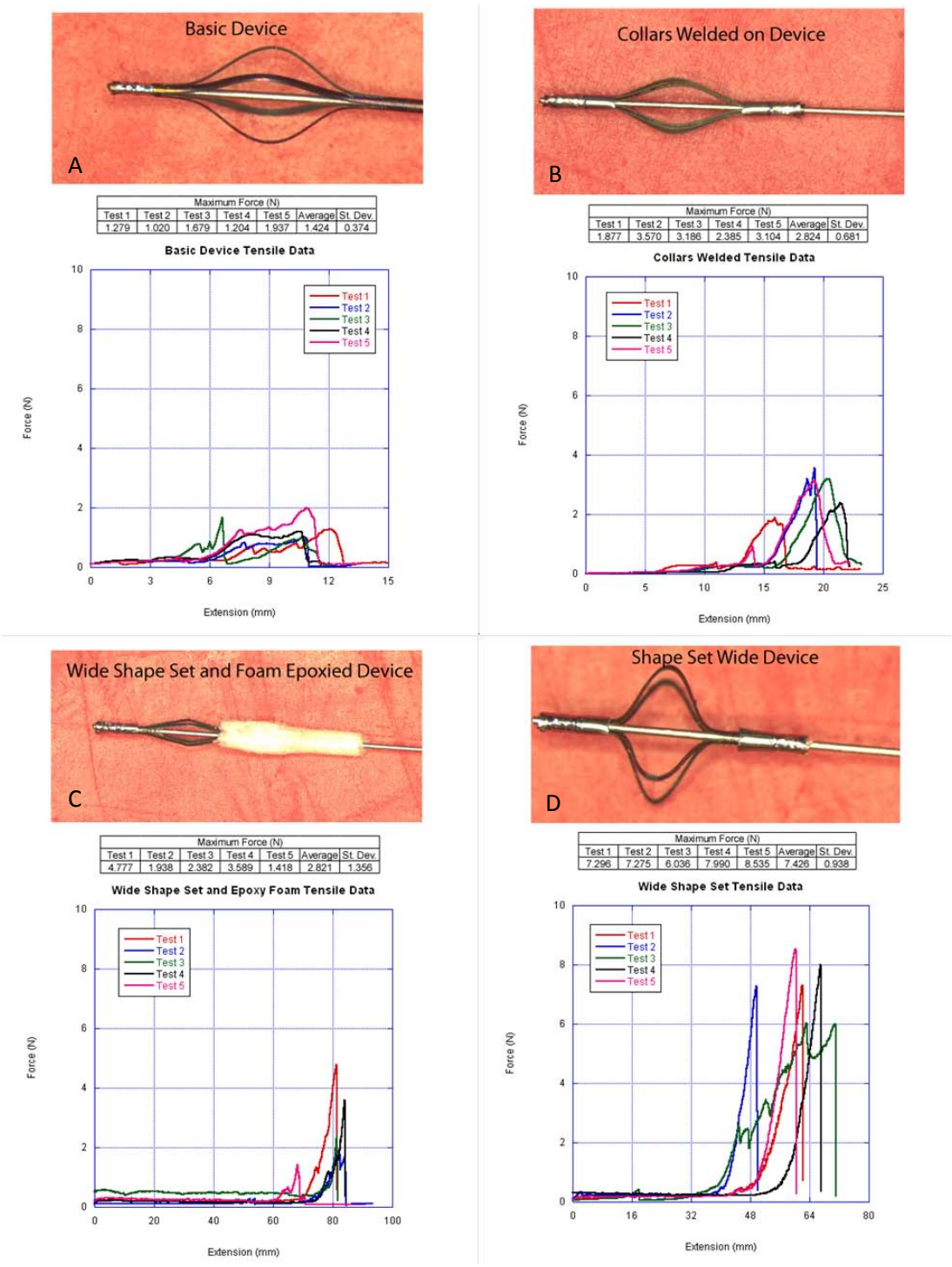

Figure 13. Images of each nitinol support piece design. Corresponding force vs. extension data and maximum force measurements for each trial are displayed underneath each image.

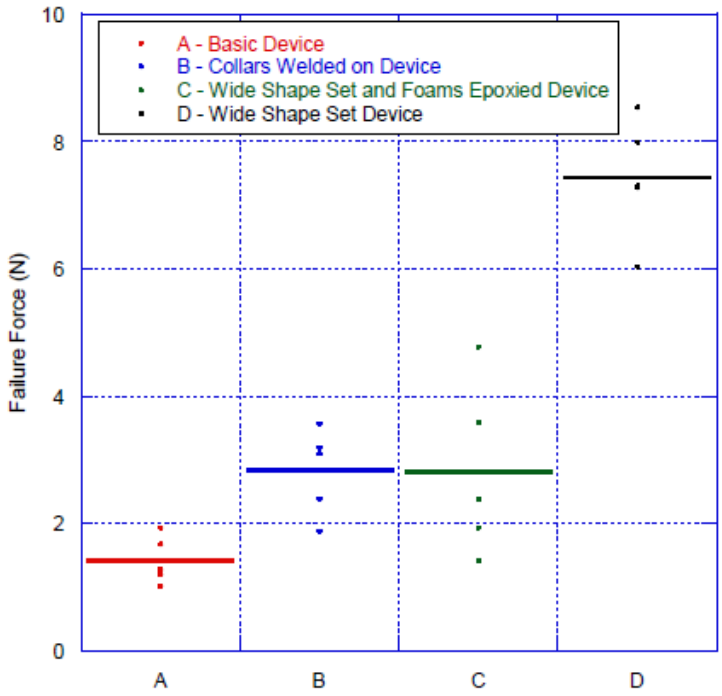

Figure 14. Maximum forces for each design. The solid bar indicates the average of the five trials' maximum forces.

In vitro thrombectomy testing

Two different sets of benchtop thrombectomy trials were attempted with the best design from tensile testing. Each successive set of tests was carried out with a completely new set of devices.

Small vessel in vitro study

For these trials, the blood clot was lodged in the smaller, 4-6 mm diameter vessel of the silicone vessel model. Five trials were attempted with retraction of the device and catheter performed by hand. The device successfully removed the blood clots past the bifurcation in the vessel model in 5/5 trials. Retraction past the bifurcation was deemed successful since at that point, a large diameter catheter could be used to aspirate the blood clot. Figure 15 shows one of the small vessel setups, with the device and catheter advanced past the blood clot. Figure 16 displays the pane-by-pane retraction of a blood clot from the small vessel by hand.

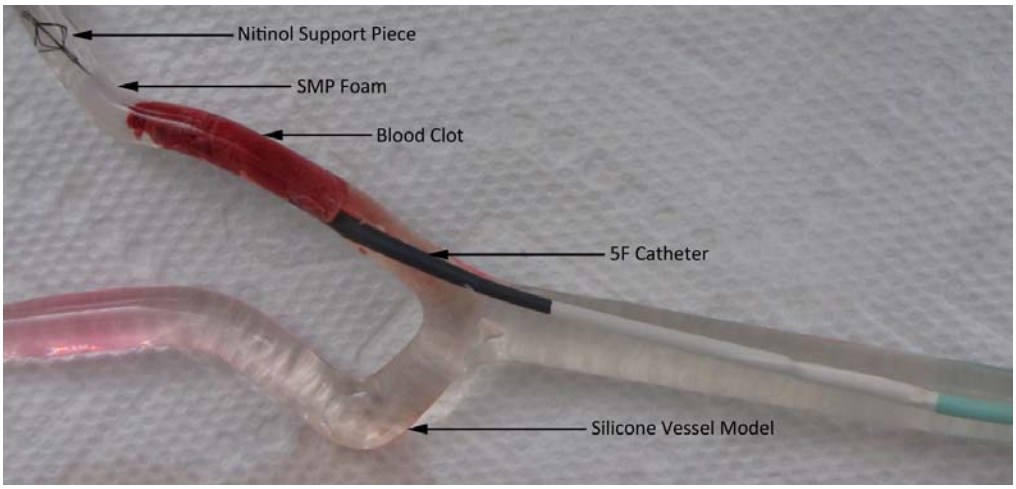

Figure 15. Device advanced past the blood clot in the smaller vessel prior to retraction. Components of the device are labeled.

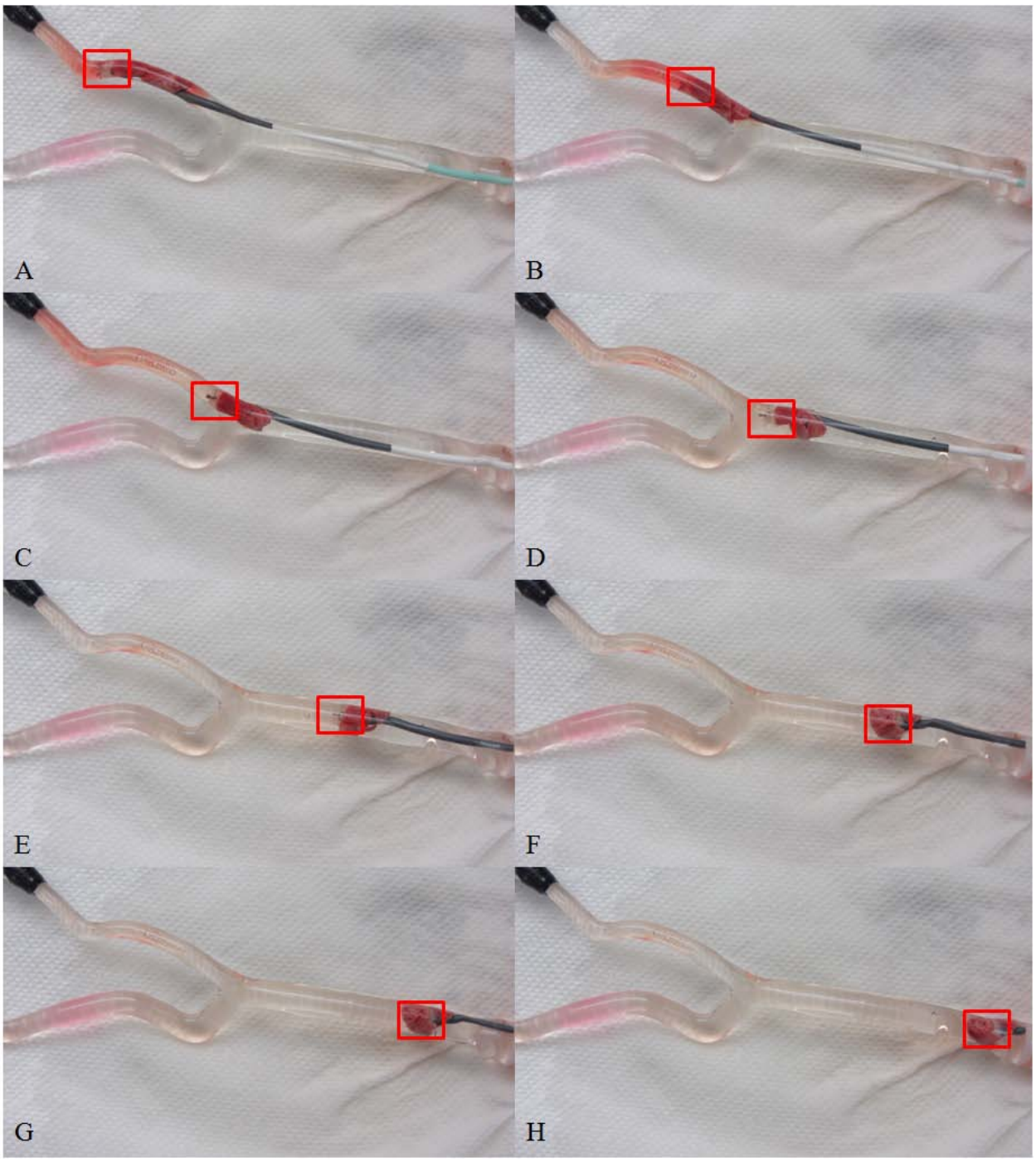

Figure 16. Successful extraction in small vessel. Red boxes trace the progress of the device across each pane. Flow was restored to the blocked vessel when the device was removed past the bifurcation in pane C. The clot compacted around the SMP foam in pane F without loss of material to distal embolization.

Large vessel in vitro study

For these trials, the blood clot was lodged in the larger, 7-8 mm diameter vessel of the silicone vessel model. Five trials were attempted with retraction of the device and catheter performed by hand. The device successfully removed the blood clot past the bifurcation in only 1/5 trials. Figure 17 shows the device and catheter advanced past a blood clot in the larger vessel model. Figure 18 illustrates the pane-by-pane attempted extraction during a failed attempt. Figure 19 displays the pane-by-pane successful extraction from the large model.

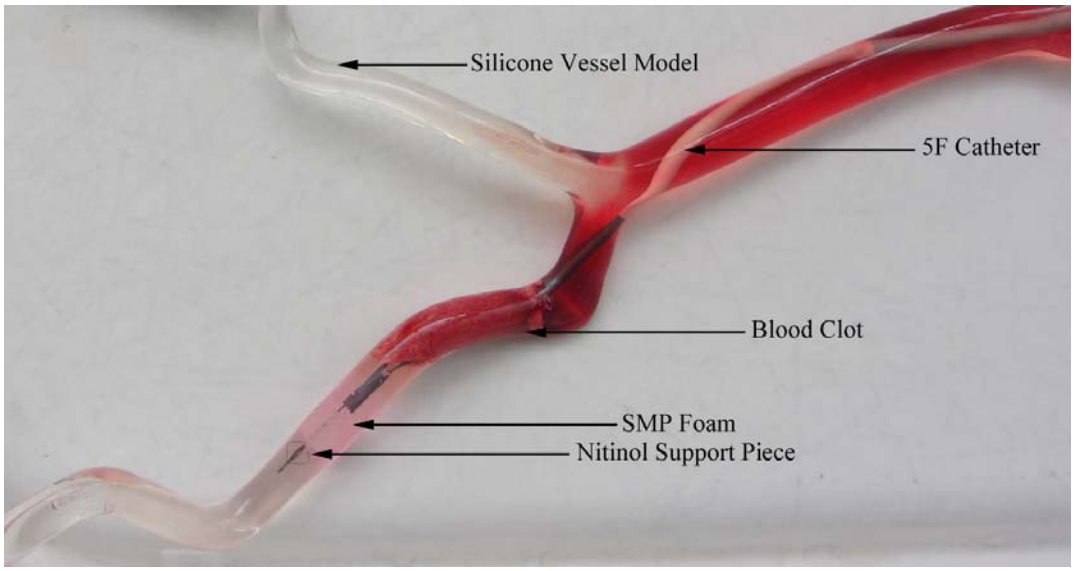

Figure 17. Device advanced past the blood clot in the large vessel prior to retraction. Components of the device are labeled.

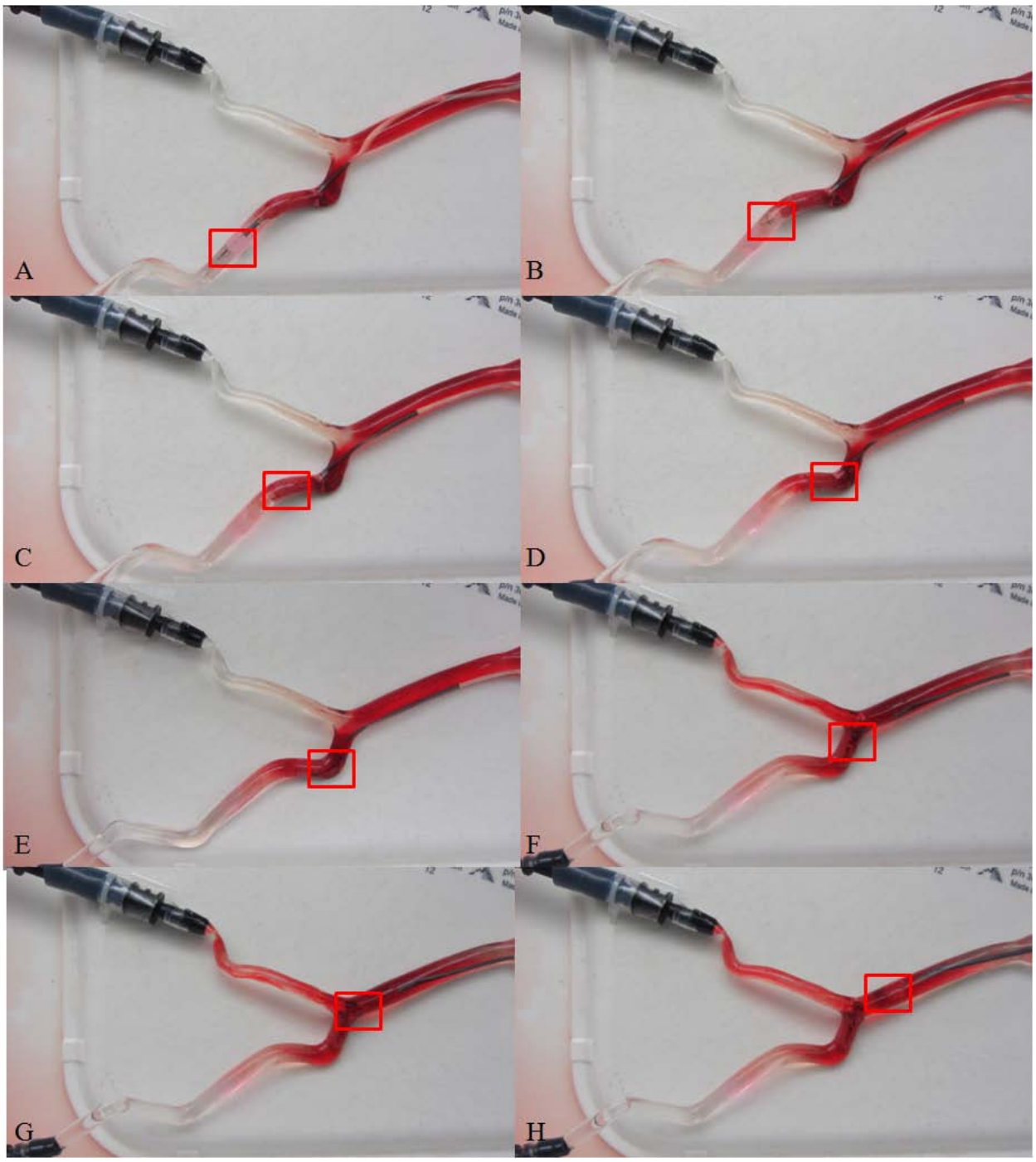

Figure 18. Failed extraction in large vessel. Red boxes trace the progress of the device across each pane. The foam pulled into the body of the clot in pane C. The clot split in half around the device in pane E. Pane H shows the device fully pulled through the clot.

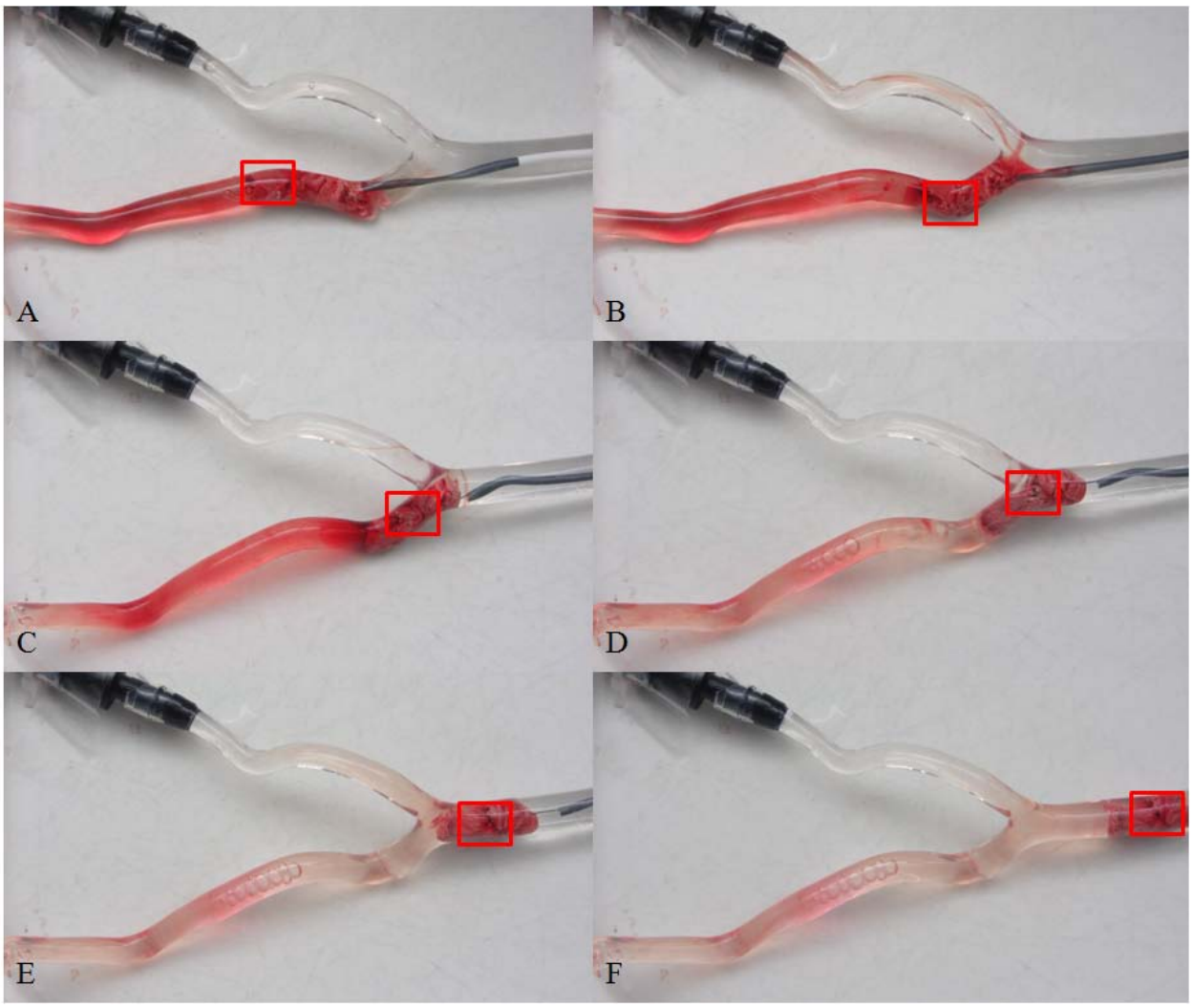

Figure 19. Successful extraction in large vessel. Red boxes trace the progress of the device across each pane. The device pulled into the blood clot in pane A. The device split the blood clot in pane C. In pane D, the clot distal to the device was held by adhesion forces to the mass of clot proximal to the device.

Retraction Force

The average retraction force across three trials was 0.69±0.32 N. The maximum force out of the three trials was 2.68 N, with the average maximum force from the three trials being 1.808±0.897 N. In comparison to the average maximum tensile strength of the design used *in vitro*, calculated to be 7.426 N, the tensile strength was more than 2.75 times higher than the maximum recorded

retraction force and was more than 10 times higher than the average retraction force. For the lowest tensile strength recorded for the design used *in vitro*, measured at 6.036 N, the tensile strength was 2.25 times the maximum recorded retraction force. Table 1 shows the force measurements for the three trials. Figure 20 shows the force vs. extension profiles for each trial.

Table 1. Force measurements for *in vitro* retraction.

	Trial 1	Trial 2	Trial 3	Average
Max Force (N)	2.684	1.848	0.892	1.808
Average Force (N)	1.429	0.297	0.343	0.690
Standard Devaition (N)	0.490	0.290	0.185	0.322

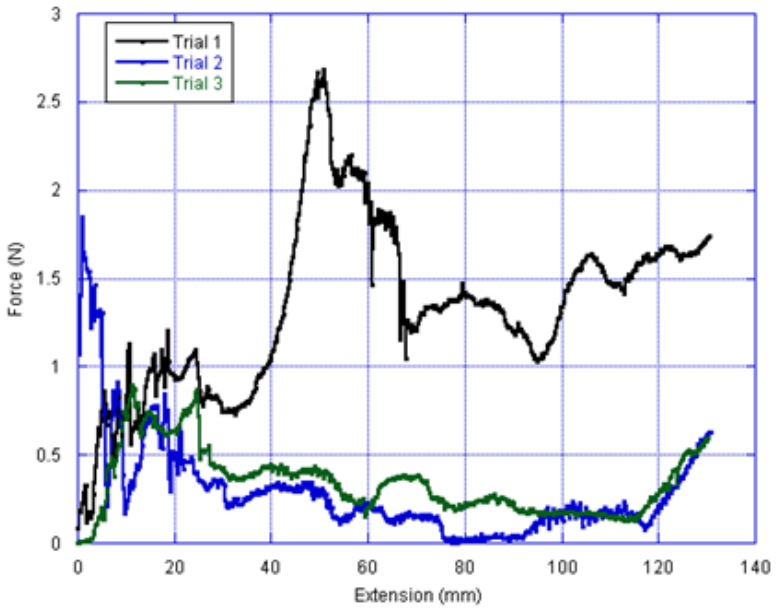

Figure 20. Force vs. extension for retraction study. The maximum force was seen in trial 1 during the motion of the device through the bifurcation.

All clots were successfully removed in these tests, for a success rate of 3/3. Figure 21 illustrates the pane-by-pane retraction of a blood clot using the tensile tester setup.

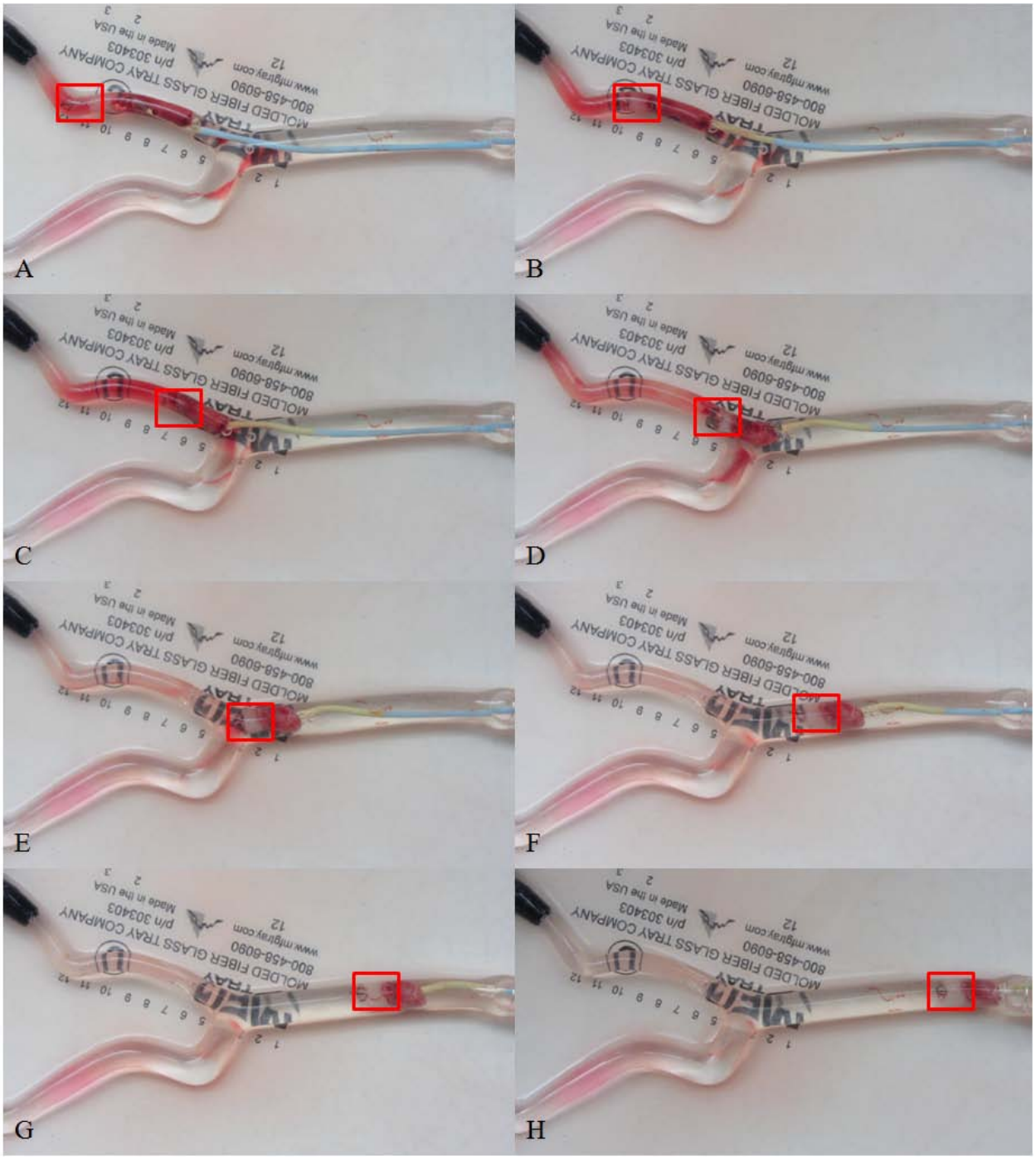

Figure 21. Retraction of blood clot and device with tensile tester. Red boxes trace the progress of the device across each pane. During this trial, the blood clot remained completely proximal to the device throughout the extraction.

Discussion

Force comparisons

A comparison of retraction force to failure force for the devices indicates that a safety factor of at least 2.25 times was present for the worst case scenario involving the peak retraction force versus the lowest failure force. Furthermore, it could be predicted that the retraction force *in vivo* would be lower due to the large amount of friction present in the tensile testing system. For an actual procedure, the number of components interfacing between the clinician and the device would be lower, with only a single Luer connection needed to control the motion of the device relative to the 5F catheter. Another important result of tensile testing was the prevention of foam loss. Early designs had the potential to lose the foam at high force values. Using epoxy to keep the foam attached was attempted as an initial solution; however, the epoxy got between the support piece and the guidewire, which caused it to get stuck as it was being compressed. Once the device stuck, the adhesion between the foam and the nitinol was not large enough to keep the foam from pulling off of the device. The alternate solution of using a larger diameter support piece proved more successful. With the larger diameter nitinol support piece, the foam was unable to come off of the device without the struts failing, which eliminated one of the device's failure modes.

In vitro studies

From the in vitro studies, it was evident that the device could be successful at retrieving blood clots from obstructed vessels. However, in the large vessel cases there were several issues seen with the retractions. When the SMP foam did not touch the whole surface of the clot, the device tended to pull into the body of the clot rather than remain distal to it. This was even evident in some of the small vessel cases once the clot expanded when it was past the bifurcation. In the

large vessel cases in particular, once the device was within the body of the clot, it tended to break into two pieces, as was evidenced in the successful large vessel extraction. Adhesion forces within the clot are helpful at keeping the thrombus together as it is retracted, but some of the early clot constructions demonstrated very weak adhesion forces and broke apart without lodging in the vessel. This means adhesion forces are often not enough to keep the clot together across the device. These considerations point to how important it is to keep the clot proximal to the device. Therefore, for future devices the foam should always be equal or greater in size compared to the obstructed vessel to make sure the device has the surface area to keep from sinking into the clot.

Another important consideration during the trials was the nitinol support piece. The support piece struts were larger in diameter than the small vessel, which made pushing the support piece far enough to get the foam out of the catheter difficult if the struts were caught on the turn in the vessel. However, maneuvering the catheter past the curve greatly simplified the delivery, and retracting the device caused the oversized struts to curve against the vessel walls. This curving of the struts helped compress the foam axially due to the larger surface of contact between the foam and the struts. The larger diameter struts also helped when the device was moving through the bifurcation, since once tension was relieved in the larger diameter of the bifurcation, the struts were free to return to their original diameter. This helped keep the foam compressed and provided more perpendicular surface area to catch clot fragments. A prime example of this case is in the small vessel extraction by hand when the clot was snared past the bifurcation by a combination of the foam and the support piece. Figure 22 shows the device during retraction with bent struts.

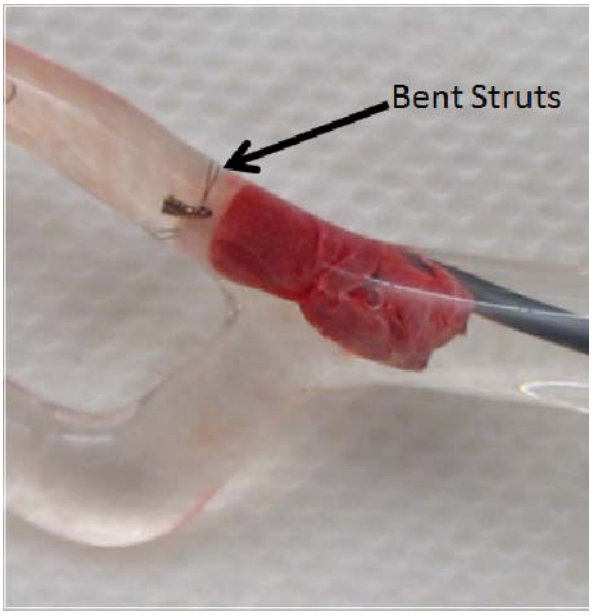

Figure 22. Curving of struts during retraction in small vessel. The bent struts cover the whole width of the vessel with the potential to recover their original diameter past the bifurcation.

The pusher performed successfully and the device never stuck in the catheter due to the foam expanding, though all delivery times for the devices were less than 10 minutes. Despite that, the foams were generally at least partially expanded when they were pushed out of the catheter, indicating that the pusher was important to keeping the foam from migrating down the guidewire. Preliminary tests during design suggested that even if the foam were left for 15 minutes to expand in body temperature water, the pusher would be able to get the foam out of the catheter. However, the diameter of the foam did limit its ability to be pushed out of the catheter. When 8 mm foam samples were left in the catheter for 15 minutes, the pusher was unable to dislodge the foam. For larger diameter vessels requiring larger diameter foams, it could be expected that a larger diameter catheter could be used, along with increased diameter tubing for the pusher. The expansion of the foam limits the range of vessels that can be treated with different diameter foams. The overall deliverability of the device with the smaller foam was an

important step forward in this device design. Previous designs used a screw mechanism along with a Teflon sheath and nitinol pusher tube, and they tended to get stuck or confused the physicians using them. Simplifying the delivery helped improve the device's ease of use.

Heat treating the guidewire did not have as much of an effect as expected. Because the catheter was kept close to the proximal end of the blood clot, the exposed section of the guidewire was typically within the body of the clot. The increased compliance of the guidewire could have helped keep the wire from disrupting the clot from inside, but catheter was close enough to help with keeping the wire centered in the vessel.

CHAPTER IV

CONCLUSION

This study focused on determining the effectiveness of an endovascular mechanical thrombectomy device with the long term goal of treating acute ischemic stroke. To characterize its effectiveness, the tensile strength, *in vitro* success rate, and retraction force were measured. Previous designs experienced tensile failure due to foam loss or strut fracture; one of the main goals of this study was to eliminate foam loss as a failure mechanism and provide a reasonable safety factor before strut failure occurred. Prevention of these device failures is vital to ensure the device does not cause distal embolization during a thrombectomy procedure. Tensile strength was compared to *in vitro* retraction force, and the device's lowest failure force proved to be 2.25 times larger than the peak retraction force seen in any trial, which suggests the device will be deployable with minimal risk of device fracture during procedures. Also, the device was redesigned to keep the foams in place at high forces, with a failure of the struts required for dislodging the foam.

In vitro studies using the device were performed with the goal of showing that the device was deliverable through a 5 F catheter and that it could retrieve a blood clot past the bifurcation in a silicone vessel model. Tests were carried out in both branches of the bifurcated model. In the smaller branch, the SMP foams were oversized to 1.5 times the vessel diameter. The device was able to retrieve the blood clots used in 8/8 trials. For the larger branch, the SMP foam was equal to or 0.75 times the size of the vessel to be treated, depending on the location within the branch. The device could only retrieve 1/5 clots lodged in this vessel, which provided valuable

information on what device specifications need to be modified for the device to perform in different applications. Successful retrievals in the smaller vessel demonstrated that the device is able to extract blood clots with a high success rate. Also, the device was able to be delivered within five minutes of catheter insertion in all cases and never became stuck in the catheter. This suggests that the device is not only effective at retrieval but is efficient and easy to use.

There were two main design goals to be met that sought to improve on currently available thrombectomy devices. The device was designed to be less than 15 mm to allow for increased maneuverability in the tortuous cerebral vasculature. Additionally, material perpendicular to the vessel was included for placement distal to the blood clot to allow for extraction of blood clots longer than the device itself. Both of these objectives were met and help distinguish this device from currently available devices.

Future work

Further validation of the device design will be carried out in two main ways. *In vitro* studies will be performed with the current FDA approved thrombectomy devices to provide a benchmark for comparison using the testing setup from this study. Additionally, animal studies will be performed using a porcine femoral artery as a model for ischemic stroke. These results will allow progression of the device towards clinical verification.

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